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Hetero-Diels-Alder Reactions of α-Nitrosoalkenes with Ferrocenyl, Hetaryl and Cycloaliphatic Thioketones

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Dedicated to Prof. Ernst Schaumann on the occasion of his 75th birthday

Abstract: The in situ generated α-nitrosoalkenes react with ferrocenyl, hetaryl and cycloaliphatic thioketones yielding 4*H*-1,5,2-oxathiazines as products of the hetero-Diels-Alder reaction. These products are formed in a perfect regioselective manner. A similar reactivity is displayed by a thiochalcone (1,3-diphenylprop-2-en-1-thione), and in that case, the [4+2]-cycloaddition occurs also chemoselectively and regioselectively along the C=S bond acting as a heterodienophile. The stability of the 4*H*-1,5,2-oxathiazines depends on the type of substituents, and in the case of ferrocenylthioketones, the diferrocenyl representative is the reagent of choice. The replacement of one ferrocenyl group by an ethyl group leads to a dramatic decrease of the product stability. Sterically crowded cycloaliphatic thioketones derived from 2,2,4,4-tetramethylcyclobutanedione are exceptional dienophiles in reactions with trifluoromethyl-substituted nitrosoalkenes, and in these cases, a remarkably stable 3-trifluoro-methyl-4*H*-1,5,2-oxathiazine derivative was obtained. For the first time, perfectly stable and non-odorous 2,2,4,4-tetramethylcyclo-butane-1,3-dithione was explored as an active heterodienophile for a two-fold hetero-Diels-Alder reaction.

Introduction

In our continuing studies on organosulfur compounds, we demonstrated in a series of recent publications that ferrocenyl, hetaryl and cycloaliphatic thioketones are versatile building blocks for the preparation of sulfur heterocycles with diverse ring sizes.[1] Cycloaddition reactions are of special importance as thioketones act as superior dipolarophiles and dienophiles. For example, ferrocenyl and hetarylthioketones react with (trimethylsilyl)-diazomethane to give 1,3,4-thiadiazolines, which spontaneously eliminate nitrogen, and the in situ generated thiocarbonyl*S*-methanide traps another molecule of the starting thioketone to give sterically crowded 4,4,5,5-tetrasubstituted 1,3-dithiolanes with complete regioselectivity.[2] The latter products, after desilylation with TBAF, are converted into tetrasubstitutedethylenes in high yields. Alkyl ferrocenylthioketones were shown to react with bis(4-methoxyphenyl)diazomethane, and after nitrogen extrusion gave the corresponding thiiranes, which via desulfurization and demethylation were converted into ferrocifens.[3] Hetaryl and ferrocenylthioketones were also used as dienophiles in asymmetric thia-Diels-Alder reactions with enantiopure trienamines leading to optically active 5,6-dihydro-2*H*-thiapyrans.[4] Interestingly, thiochalcones react as heterodienes with the terminal C=C group of dienamines to give 3,4-dihydro-2*H*-thiapyrans.[5]

Based on kinetic studies, aromatic thioketones were named 'superdipolarophiles' and reacted smoothly with non-activated dienes such as 2,3-dimethylbuta-1,3-diene and (*E,E*)-hexa-2,4-diene forming the corresponding 5,6-dihydro-2*H*-thiopyrans.[6] Hetarylthioketones behave similarly, and reactions with non-activated dienes could be performed at room temperature.[7] In that case, a non-concerted mechanism of the [4+2]-cycloaddition was observed.An interesting class of heterodienes consist of α-nitrosoalkenes**1**, which typically are generated in situ by 1,4-dehydrohalogenation of differently substituted α-halooximes**2** (Scheme 1).[8] In an alternative protocol, a formal 1,2-elimination of HCl from α-chloronitroso-1-arylethanes **3** was reported as a straightforward access to α-nitrosoalkenes.[9] The high electrophilicity of conjugated nitrosoalkenes was also studied by means of computational methods.[10] Since many years they have been used mainly as electron-deficient heterodienes for [4+2]-cycloadditions with alkenes[11,12] and allenes[13] yielding the respective 1,2-oxazine derivatives **4** and **5**.

In a previous publication, reactions of 1-aryl-1-nitrosoethenes with thiobenzophenone and its derivatives were reported to yield 4*H*-1,5,2-oxathiazines **6** in a regioselective manner.[14] In addition, dithiobenzoate and diphenyl trithiocarbonate were used as efficient heterodienophiles.[14] Similar reactions with silylatedthioketones [Ph(R_3Si)C=S] were also performed.[14,15]

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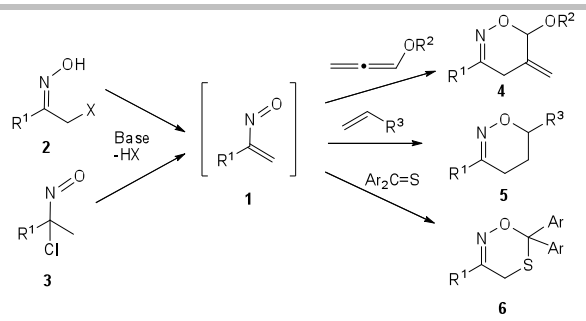


Scheme 1. Typical methods for the generation of α-nitrosoalkenes **1** and their reactions with alkoxyallenes, alkenes, and diarylthioketones.

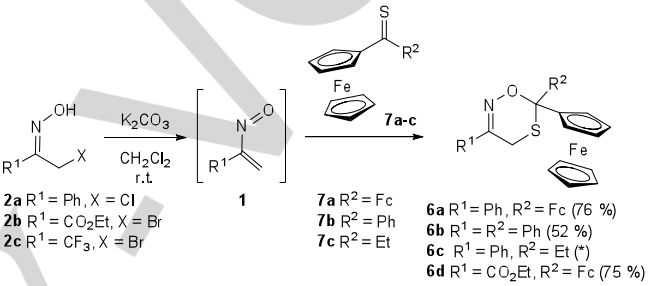
Efficient methods for the preparation of relatively stable and non-odorous aryl/hetaryl-, dihetaryl- and ferrocenyl-substituted thioketones[1] motivated us to perform thia-Diels-Alder reactions with differently substituted α-nitrosoalkenes **1** bearing a Ph, CF_3, CO_2Et or CH=CH-CO_2Me group. In addition, aliphatic thioketones and a thiochalconewere used for the first time as heterodieonophiles. The goal of the present study was the synthesis of hitherto unknown 1,5,2-oxathiazine derivatives, and those containing a ferrocenyl substituent are of special interest for further applications.

Results and Discussion

Additions In the first part of the study, reactions of ferrocenylthioketones **7a**–**c** with 1-nitroso-1-phenylethene (**1a**) were tested in order to establish scope and limitation of [4+2]-cycloadditions leading to ferrocenyl-substituted 4*H*-1,5,2-oxathiazines **6a**–**c**. The test experiment was performed starting with diferrocenylthioketone (**7a**) and α-chloroacetophenone oxime (**2a**) in dichloromethane in the presence of potassium carbonate at room temperature. The progress of the reaction was monitored by TLC and the change of the color of the solution. After 30 min, the characteristic violet color of **7a** vanished and **7a** could not be detected by the TLC test. The chromatographic workup led to a yellow solid in 76 % yield, which was identified as the expected [4+2]-cycloadduct**6a** (Scheme 2). The spectroscopic data confirmed its structure, and in the ^{1}H NMR spectrum, the characteristic signal of the CH_2 group was located at 3.45 ppm. The ^{13}C NMR spectrum revealed the absorption of this group at 23.3 ppm. In addition, signals attributed to C(3)=N and C(6) were found at 157.8 and 86.7 ppm, respectively.

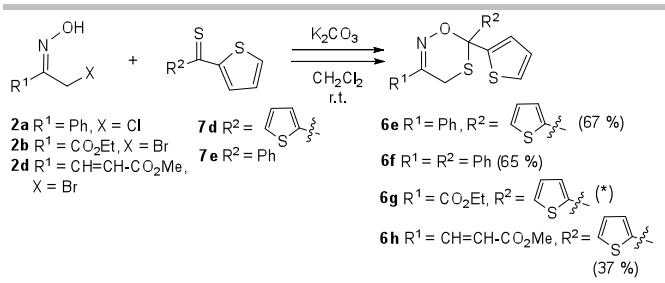
Similarly, the reaction of **2a** with ferrocenyl phenyl thioketone (**7b**) afforded also only one product identified as **6b**. In that case, the diagnostic signal for the CH_2 group appeared in the ^{1}H NMR spectrum as an AB system at 3.22 and 3.53 ppm (J = 17.6 Hz). In the third experiment, ethyl ferrocenylthioketone (**7c**) was used, but in that case, the initially formed cycloadduct was unstable and an analytically pure sample could not be isolated. However, the predicted structure was confirmed by ^{1}H and ^{13}C NMR spectra. Again, the diagnostic C(4)H_2 signal was found in the ^{1}H NMR spectrum as an AB system (3.52 and 3.65 ppm, J = 16.1 Hz) along with two multiplets located at 2.21–2.27 and 2.34–2.40 ppm attributed to two diastereotopic H-atoms of the ethyl CH_2 group. These results point out that the presence of an additional ferrocenyl or phenyl residue enhances the stability of 2-ferrocenyl-substituted 4*H*-1,5,2-oxathiazines **6**.

Diferrocenylthioketone (**7a**) was tested also in reactions with α-nitrosoalkenes generated from ethyl 3-bromo-2-hydroxyiminopropionate (**2b**) and 3-bromo-1,1,1-trifluoro-2-hydroxyiminopropane (**2c**). In the first case, the [4+2]-cycloaddition afforded the desired product **6d** in 75 % yield as a stable compound (Scheme 2). In the second case, however, the color of the reaction mixture turned to black within a few minutes and no defined products could be isolated.



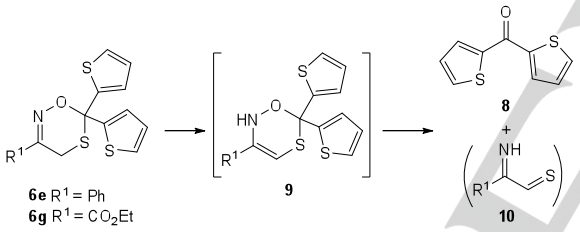
Scheme 2. Reaction of α-nitrosoalkenes**1** generated from α-halooximes**2a**–**c** with ferrocenylthioketones**7a**–**c** leading to 6-ferrocenyl-4*H*-1,5,2-oxathiazines **6a**–**d** (Fc = ferrocenyl; *not isolated in pure form).

The second group of thioketones involved in this study consisted of hetarylthioketones, such as bis(thiophen-2-yl) thioketone (**7d**) and phenyl thiophen-2-yl thioketone (**7e**). In both cases, the reactions of α-nitrosostyrene (in situ generated from precursor **2a**) led to thienyl-substituted 4*H*-1,5,2-oxathiazines **6e** and **6f**, respectively (Scheme 3). In analogy to the previously described products **6a** and **6b**, the signal of the C(4)H_2 group appeared in the ^{1}H NMR spectra as a singlet at 3.70 ppm in **6e** and as an AB-system at 3.49 and 3.65 ppm (J = 17.6 Hz) in **6f**. Notably, the cycloadduct**6e** underwent a slow decomposition during the storage in $CDCl_3$ solution at room temperature, and bis(thiophen-2-yl) ketone (**8**) was identified as decomposition product. The bis(thiophen-2-yl) thioketone (**7d**) was also reacted with **2b** as well as with methyl 5-bromo-4-hydroxyiminopent-2-enoate (**2d**). Whereas the reaction with **2d** led to a stable cycloadduct**6h** in moderate yield (37 %), the product **6g** derived from **2b** could only be identified spectroscopically in the crude mixture. Decomposition during chromatographic work-up was observed and the isolation of an analytically pure sample of **6g** was unsuccessful. Again the bis(thiophen-2yl) ketone (**8**) was detected as the major product of the decomposition process.



Scheme 3. Reaction of α-nitrosoalkenes with thiophen-2-yl thioketones **7d** and **7e** (* not isolated in pure form).

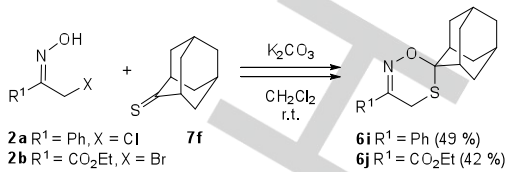
A plausible reaction mechanism for the formation of bis(thiophen-2-yl) ketone (**8**) from the cycloadducts**6e** and **6g** is shown in Scheme 4. Imine-enamine tautomerization can lead to intermediate **9**, which undergoes a retro-hetero-Diels-Alder reaction to give thioketone**8** and highly reactive α-iminothioaldehyde**10**.[16] The latter may decompose further under the reaction conditions, but its existence could not be evidenced either spectroscopically in the crude mixture or by isolation in monomeric or oligomeric form. Moreover, attempted trapping of the postulated **10** with thiobenzophenone, added in excess as a 'superdienophilic agent' to the solution of **6e** in $CDCl_3$ at room temperature, was unsuccessful.



Scheme 4. Proposed reaction mechanism for the formation of bis(thiophen-2-yl) ketone (**8**) from 4*H*-1,5,2-oxathiazines **6e** and **6g**.

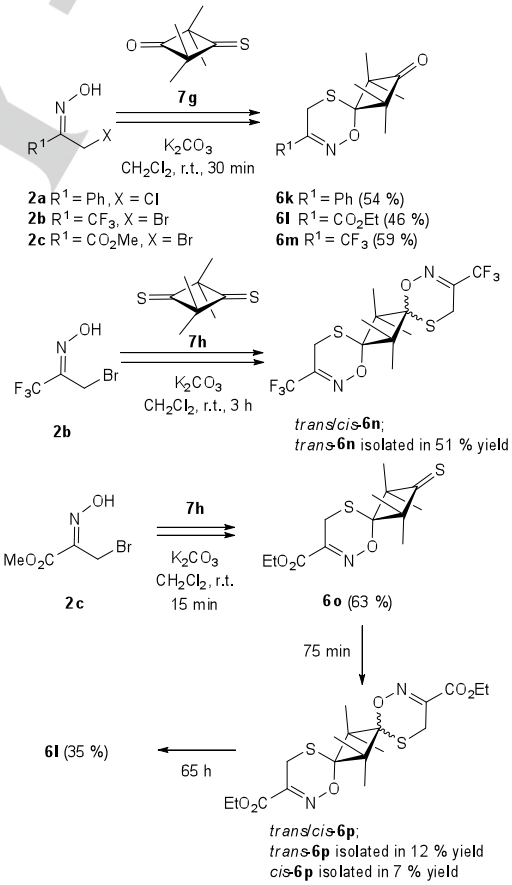
The sulfur-rich cycloadduct**6e**was selected for the attempted oxidation with an excess of *m*-chloroperbenzoic acid in CH_2Cl_2 solution at room temperature. Under these conditions, in analogy to a reported similar experiment with a 6,6-bis(*p*-tolyl) analogue,[14] only decomposition of the compound was observed.

Adamantanethione (**7f**), 3-thioxo-2,2,4,4-tetramethylcyclobutanone (**7g**) as well as 2,2,4,4-tetramethylcyclobutane-1,3-dithione (**7h**) are widely explored as representatives of cycloaliphatic thioketones.[17] In a very recent report, thioketone **7g** was used in reactions with 'donor-acceptor cyclopropanes' in the presence of a Lewis-acid, and tetrahydrothiophene derivatives, which are formally derived from dimethylthioketene were obtained in good yields.[18] In the present study, the reactions of thioketone **7f** with **2a** and **2b** gave the expected spiro compounds **6i** and **6j** in fair yields (Scheme 5). In these symmetrically substituted products, the diagnostic ^{1}H NMR signals of the C(4)H_2 groups were found as singlets at 3.52 and 3.51 ppm, respectively. In the ^{13}C NMR spectra, the absorptions of C(3)=N and C(6) of the heterocyclic ring appeared at 168.5/95.2 and 147.6/89.9 ppm, respectively. The attempted reaction with the fluorinated precursor **2c** was unsuccessful.



Scheme 5. Reactions of α-nitrosoalkenes with adamantanethione (**7f**).

A series of experiments was performed with the sterically crowded thioketones **7g** and **7h**, which yielded remarkably stable 4*H*-1,5,2-oxathiazines including trifluoromethyl-substituted derivatives. The mono-thioketone **7g** was reacted with α-nitrosoalkenes derived from **2a**–**c**, and in all cases, the expected cycloadducts **6k**–**m** were obtained as stable compounds (Scheme 6). In all three products, the characteristic absorptions of the C=O group were found at 1785–1778 cm^{-1} in the IR spectra and at 217.7 ppm in the ^{13}C NMR spectra.



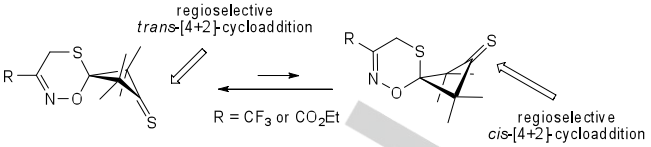
Scheme 6. Reactions of α-nitrosoalkenes **2** with monothione **7g** and dithione **7h**; formation of mono- and bis-spiro-cycloadducts **6**.

The dithioketone **7h** was combined with the precursors **2b** and **2c**, used in 4-fold excess, under the usual conditions, and in the

case of **2b** the bis-spiro product **6n** was obtained as *trans*/*cis*-mixture (3:1) after 3 h (Scheme 6). The assignments of *cis*- and *trans*-bis-cycloadducts of type **6** was based on the ^{1}H NMR data. Whereas in the case of *trans*-isomers only one signal for four methyl groups appears, two signals are diagnostic for *cis*-isomers. The pure major product *trans*-**6n** was isolated chromatographically in 51 % yield and the singlet attributed to all four methyl groups was found at δ 1.39 ppm.

The progress of the similar reaction of **7h** with **2c** and the type of the products formed after different reaction times were checked carefully by ^{1}H NMR control of the crude mixtures and identification of the isolated major products. Thus, after 15 min at room temperature, the major component of the reaction was identified as the mono-cycloadduct **6o**, which was separated chromatographically in 63 % yield. In the ^{13}C NMR spectrum, the diagnostic signal of the C=S group was found at δ 276.0 ppm and the correct elemental analysis confirmed the molecular formula $C_{13}H_9NO_3S_2$. After a longer reaction time (75 min), the expected mixture of *trans*- and *cis*-cycloadducts **6p** in a ratio of ca. 65:35 was obtained. After chromatographic work-up, both isomers were isolated as pure compounds and the spectroscopic data confirmed unambiguously their structures. In the case of *trans*-**6p**, the signal of four equivalent methyl groups appeared as a singlet at δ 1.38 ppm, and two CH_2 groups were found at δ 3.58 ppm. Finally, in a long time experiment, which was performed within 65 h at room temperature, the already known cycloadduct **6l**, obtained in the reaction of **7g** with **2c**, was found as the major component of this mixture. It was subsequently isolated as a pure compound in 35 % yield (Scheme 6). Apparently, it was formed after slow decomposition of the bis-cycloadducts **6p**, analogous to those observed in the reaction with di(thiophen-2-yl) thioketone (**7d**) and presented in Scheme 4.

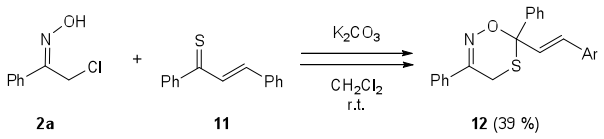
Bis-cycloadducts **6n** and **6p** are the first examples of two-fold [4+2]-cycloadducts obtained via Diels-Alder reactions starting with **7h**. This useful, stable and non-odorous dithione has extensively been explored in 1,3-dipolar cycloadditions,[17c] and in most cases formation of mixtures of five membered *trans*- and *cis*-bis-cycloadducts was observed. However, depending on the type of the 1,3-dipole used, either the *cis*- or *trans*-isomer predominated in the mixture. For example, in the case of diazomethane, the *trans*-isomer of the formed bis-1,3-4-thiadiazoline was the major product (*trans*/*cis* ratio ca. 3:1),[19a] but the bulky di-*tert*-butyl diazomethane gave the *trans*-bis-cycloadduct exclusively.[19b] On the other hand, an electron deficient nitrile imine derived from trifluoroacetonitrile gave the *cis*-isomer as the only bis-[3+2]-cycloadduct in the reaction with **7h** in moderate yield.[19c] The preferred formation of the *trans*-bis-cycloadducts**6n** and **6p,** observed in the present study, can be plausibly explained by the sterically less crowded transition state, which governs the direction of the second [4+2]-cycloaddition as illustrated in Scheme 7.



Scheme 7. Two competitive [4+2]-cycloadditions leading to isomeric bis-cycloadducts **6n** or **6p**; in both cases mixtures of *cis*- and *trans*-isomers are formed.

In extension of our study, thiochalcone **11** was also investigated preliminarily in reaction with the conjugated nitrosoalkene generated from **2a**. In earlier publications, we reported hetero-Diels-Alder reactions with thiochalcones reacting not only as heterodienes with C=C[5] and C≡C[20] bonds, but also as the C=S dipolarophiles in 1,3-dipolar cycloadditions with electron deficient, fluorinated nitrile imines.[21] It is also worth mentioning that thiochalcones exist in solution in equilibrium of the monomeric and two dimeric forms, which result from two types of thia-Diels-Alder reactions.[21,22] For these reasons, it was attractive to study which type of reactivity will dominate as both reactants, **11** and the in situ generated **1**, can act either as diene or dienophile.[23]

The experiment performed with **2a** and (*E*)-1,3-diphenylprop-2-en-1-thione (**11**) in CH_2Cl_2 in the presence of K_2CO_3 at room temperature led to cycloadduct **12** in a chemo- and regioselective manner (Scheme 8). Thus, in analogy to thioketones**7**, the C=S group of the monomeric **11** reacted as dienophile with the conjugated α-nitrosoalkene. A characteristic feature of the ^{1}H NMR spectrum was the presence of two AB-systems at 3.45 and 3.65 ppm (J = 17.4 Hz) and 6.63 and 6.77 ppm (J = 15.9 Hz) for the CH_2 and (*E*)-CH=CH units, respectively. The ^{13}C NMR spectrum showed a pattern of signals characteristic for the [4+2]-cycloadducts of general structure **6**, e.g., the C=N group absorbed at 152.2 ppm, the C(6) atom at 86.9 ppm, and the CH_2 moiety at 23.4 ppm.



Scheme 8. Chemo- and regioselective hetero-Diels-Alder reactions of the α-nitrosoalkene derived from **2a** with thiochalcone **11**.

Conclusions

The present study shows that not only thiobenzophenone derivatives but also ferrocenyl, hetaryl and cycloaliphatic thioketones as well as an α,β-unsaturated thioketone react with conjugated α-nitrosoalkenes as active C=S heterodienophiles. The observed [4+2]-cycloadditions occur with perfect regioselectivity, and in the case of a thiochalcone, also chemoselectively. The obtained 4*H*-1,5,2-oxathiazines show variable stability depending on the type of substituents. For the

first time, hetero-Diels-Alder reactions were performed with dithione **7h**, which gave with the CF_3- and CO_2Et-substituted α-nitrosoethylenes the expected [4+2]-cycloadducts as mixtures of *cis*- and *trans*-isomers with the latter one as the major component in both cases. Remarkably, the stable trifluoromethyl-substituted mono- and bis-cycloadducts**6m** and **6n** were obtained with sterically crowded 3-thioxo-2,2,4,4-tetramethylcyclobutanone (**7g**) and 2,2,4,4-tetramethylcyclobutane-1,3-dithione (**7h**), respectively. The target products, i.e. 4*H*-1,5,2-oxathiazines **6**, belong to a class of less explored six-membered heterocycles, and the presented method for their synthesis based on a thia-Diels-Alder approach offers a useful access to these heterocyclic compounds. The desired selection of the thioketones and of the conjugated α-nitrosoalkenes enables the introduction of diverse substituents into the six-membered ring, which can be of importance for potential applications of these heterocycles. The chemoselective [4+2]-cycloadditon of thiochalcone **11** opens access to novel, 6-styryl functionalized 4*H*-1,5,2-oxathiazines, which can be further functionalized along the C=C bond. This part of the study requires further work with extension to differently substituted (hetaryl, ferrocenyl) thiochalcones and computational investigations in order to understand the observed chemoselectivity. In general, the heterocycles described in the present study may be of potential interest as biologically active compounds, in particular the novel fluoroalkyl-substituted derivatives. On the other hand, electroactive ferrocenyl derivatives are interesting systems for materials chemistry. Finally, due to the presence of N, O and S atoms, known as metal complexing centers, they can be applied as a new type of ligands for coordination chemistry.

Supporting Information Summary

Details onthe synthesis and characterization of the prepared substances and their ^{1}H and ^{13}C NMR spectra are provided in the Supporting Information.

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Keywords: Heterocyclic compounds •α-nitrosoalkenes•4*H*-1,5,2-oxathiazines •thia-Diels–Alderreactions •thioketones

[1] G. Mlostoń, P. Grzelak, R. Hamera-Fałdyga, M. Jasiński, P. Pipiak, K. Urbaniak, Ł. Albrecht, J. Hejmanowska, H. Heimgartner, *Phosphorus Sulfur Silicon Relat. Elem.* **2017**, *192*, 204–211.

[2] G. Mlostoń, R. Hamera-Fałdyga, A. Linden, H. Heimgartner, *Beilstein J. Org. Chem.* **2016**, *12*, 1421–1427.

[3] G. Mlostoń, R. Hamera-Fałdyga, M. Celeda, H. Heimgartner, *Org. Biomol. Chem.* **2018**, *16*, 4350–4356.

[4] J. Hejmanowska, M. Jasiński, G. Mlostoń, Ł. Albrecht, *Eur. J. Org. Chem.* **2017**, 950–954.

[5] J. Hejmanowska, M. Jasiński, J. Wojciechowski, G. Mlostoń, Ł. Albrecht, *Chem. Commun.* **2017**, *53*, 11472–11475.

[6] U. Rohr, J. Schatz, J. Sauer, *Eur. J. Org. Chem.* **1998**, 2875–2883.

[7] G. Mlostoń, P. Grzelak, A. Linden, H. Heimgartner, *Chem. Heterocycl. Compd.* **2017**, *53*, 518–525.

[8] a) T. L. Gilchrist, *Chem. Soc. Rev.* **1983**, *12*, 53–73; b) I. M. Lyapkalo, S. L. Ioffe, *Russ. Chem. Rev.* **1998**, *67*, 467–484; c) H.-U. Reissig, R. Zimmer, *1-Nitrosoalkenes*, in: *Science of Synthesis*, **2006**, Vol. 33, 371–389 and in *Science of Synthesis (Knowledge Update)* **2015/2**, 315–334, ThiemeVerlag, Stuttgart.

[9] R. K. Yahya, N. U. Kudva N., K. M. L. Rai, *Int. J. Chem.* **2014**, *6*, 26–34.

[10] a) D. Sperling, A. Mehlhorn, H.-U. Reissig, J. Fabian, *Liebigs Ann.* **1996**, 1615–1621; b) J. Liu, S. Niwayama, Y. You, K. N. Houk, *J. Org. Chem.* **1998**, *63*, 1064–1673; c) L. R. Domingo, M. T. Picher, P. Arroyo, *Eur. J. Org. Chem.* **2006**, 2570–2580; d) L. Domingo, P. Perez, J. A. Sáez, *RSC Adv.***2013**, *3*, 1486–1494.

[11] a) R. Faragher T. L. Gilchrist, *J. Chem. Soc., Perkin Trans. 1*, **1979**, 249–257; b) D. E. Davies. T. L. Gilchrist. T. G. Roberts. *J. Chem. Soc., Perkin Trans. 1*, **1983**, 1275–1281; c) T. L. Gilchrist, T. G. Roberts, *J. Chem. Soc., Perkin Trans. 1*, **1983**, 1283–1292.

[12] a) C. Hippeli, H.-U. Reissig, *Liebigs Ann. Chem.* **1990**, 217–226; b) H.-U. Reissig, C. Hippeli, T. Arnold, *Chem. Ber.* **1990**, *123,* 2403–2411; c) T. Arnold, B. Orschel, H.-U. Reissig, *Angew. Chem.* **1992**, *104*, 1084–1086; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1033–1035; d) R. Zimmer, H.-U. Reissig, *J. Org. Chem.* **1992**, *57*, 339–347; e) R. Zimmer, M. Collas, M. Roth, H.-U. Reissig, *Liebigs Ann.* **1992**, 709–714; f) R. Zimmer, M. Collas, R. Czerwonka, U. Hain, H.-U. Reissig, *Synthesis* **2008**, 237–244.

[13] a) R. Zimmer, H.-U. Reissig, *Angew. Chem.* **1988**, *100*, 1576–1577; *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 1518–1519; b) R. Zimmer, H.-U. Reissig, *Liebigs Ann. Chem.* **1991**, 553–562.

[14] B. F. Bonini, E. Foresti, G. Maccagnani, G. Mazzanti, P. Sabatino, P. Zani, *Tetrahedron Lett*. **1985**, *26*, 2131–2134.

[15] P. Carisi, G. Mazzanti, P. Zani, G. Barbaro, A. Battaglia, P. Giorgianni, *J. Chem. Soc., Perkin Trans. 1*, **1987**, 2647–2651.

[16] For related fragmentations of 1,2-oxazine derivatives, see: a) P. Bravo, G. Gaudiano, P. P. Ponti, A. Umani-Ronchi, *Tetrahedron* **1970**, *26*, 1315–1330; b) S. Shatzmiller, A. Eschenmoser, *Helv. Chim. Acta* **1973**, *56*, 2975–2981; c) C. Hippeli, R. Zimmer, H.-U. Reissig, *Liebigs Ann. Chem.* **1990**, 469–474.

[17] a) H. Heimgartner, G. Mloston, J. Romanski, in 'Electronic Enzyclopedia of Reagents in Organic Synthesis', L. Paquette, J. Rigby, D. Crich and P. Wipf, eds., John Wiley & Sons, Chichester, West Sussex, **2005**, PO19 8SQ, UK, Article RN00504; b) H. Heimgartner, G. Mloston, in 'Electronic Enzyclopedia of Reagents in Organic Synthesis', L. Paquette, J. Rigby, D. Crich and P. Wipf, eds., John Wiley & Sons, Chichester, West Sussex, **2003**, PO19 8SQ, UK, Article RN00429; c) H. Heimgartner, G. Mloston, in 'Electronic Enzyclopedia of Reagents in Organic Synthesis', L. Paquette, J. Rigby, D. Crich and P. Wipf, eds., John Wiley & Sons, Chichester, West Sussex, **2003**, PO19 8SQ, UK, Article RN00430.

[18] A. U. Augustin, M. Busse, P. G. Jones, D. B. Werz, *Org. Lett.* **2018**, *20*, 820–823.

[19] a) G. Mlostoń, M. Celeda, A. Linden, H. Heimgartner, *Polish J. Chem.***2004**, *78*, 2089–2099; b) P. J. Garret, D. Payne, D. A. Tocher, *J. Org. Chem.***1990**, *55*, 1909–1915; c) G. Utecht, J. Sioma, M. Jasiński, G. Mlostoń, *J. Fluorine Chem.***2017**, *201*, 68–75.

[20] G. Mlostoń, P. Grzelak, H. Heimgartner, *J. Sulfur Chem.* **2017**, *38*, 1–10.

[21] P. Grzelak, G. Utecht, M. Jasiński, G. Mlostoń, *Synthesis* **2017**, *49*, 2129–2137.

[22] a) T. Karasaka, S. Motoki, *J. Org. Chem.* **1978**, *43*, 4147–4150; b) T. Karasaka, S. Motoki, *J. Org. Chem.* **1979**, *44*, 4151–4155; c) H. Tanaka, S. Motoki, *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2047–2049.

[23] For a related system involving 1,3-dienes and an α-nitrosoalkene, see: A. A. Tishkov, I. M. Lyapkalo, S. L. Ioffe, *Org. Lett.* **2000**, *2*, 1323–1324.

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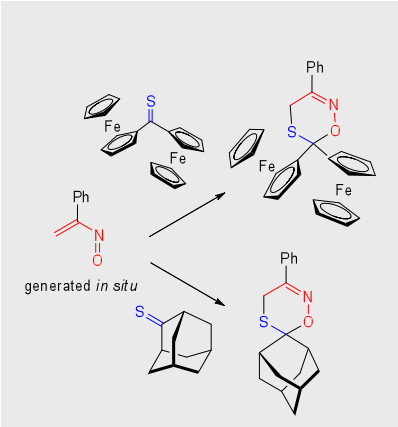
Hetero-Rich Cycles

The Diels-Alder reactions of in situ generated α-nitrosoalkenes to aryl, hetaryl and cycloaliphatic thioketones occur with complete regioselectivity providing 4*H*-1,5,2-oxathiazines in good yield. The electroactive, ferrocenyl-substituted six-membered heterocycles prepared thereby are of special interest.



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